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Letter to the Editor

Refined Genetic Mapping of X-Linked Thoracoabdominal Syndrome

To the Editor:

We have previously described thoracoabdominal syndrome [TAS; Carmi et al., 1990] and mapped the gene to Xq25-26 [Parvari et al., 1994]. After using new polymorphic markers made available since the previous publication, and detecting a reading error of one allele of a CA repeat at the DXS102 locus in one individual in the affected family, we refined the localization of TAS to Xq27, with no recombination observed with DXS1232 and DXS984.

Microsatellite polymorphic loci available for the Xq25-q27 interval were tested on the 27 relatives of the TAS family. Linkage between the TAS locus and marker loci was calculated using ILINK and MLINK from the Linkage program v5.1 [Lathrop et al., 1984]. The TAS locus was modeled as an X-linked dominant locus with full penetrance. The pairwise linkage data for the informative markers on Xq25-q27 are presented in Table I. The highest lod scores of 5.49 and 6.36 were obtained for DXS1232 and DXS984, respectively, at theta = 0. The first neighboring loci showing one cross-over were F9 on the centromeric side and DXS1205 on the telomeric side (the latter showing a different recombination event). The estimated genetic distance between these flanking loci is about 5 cM and the physical distance is 2.5 Mb (±100 Kb) [Little et al., 1991; Zucchi et al., manuscript in preparation]. In addition to the loci presented in Table I the following loci were tested and found to be noninformative: DXS1062, DXS1211, DXS998, DXS1215, DXS1193 [Gyapay et al., 1994], and AFM144yd2 (Genethon). Additional uninformative restriction fragment length polymorphism (RFLP) loci tested included: DXS105 (probe cX55, DNA digested with EcoR I, Taq I, and Hind III) [Hofker et al., 1985]; DXS 152 (probe cX33.2, DNA digested with ApaL I) [Hofker et al., 1985]; and DXS 119 (probe 780, DNA digested with Bcl I) [Hofker et al., 1985]. The results presented here thus narrow down the region for the search for the TAS gene to an interval of about 2.5 Mb. SOX3, a gene related to SRY and expressed in mouse embryonal tissues, has been mapped to this interval [Stevanovich et al., 1993] and is a candidate gene. Genes for several other disorders have been localized in the vicinity of the TAS interval. Among them are premature ovarian failure with a deletion of Xq26.1-28 presenting with no other abnormalities [Tharapel et al., 1993]; split hand split foot in Xq26.1 [Faiyaz ul Haque et al., 1992]; Simpson-Golabi-Behmel syndrome in Xq25-27 [Xuan et al., 1994]; and a heterotaxy gene has also been placed somewhere in Xq24-q27 [Casey et al., 1993]. This latter condition of faulty body lateralization is of special interest in our context, since midline formation and body placement determination are developmentally related blastogenetic events. It is conceivable that the region Xq24-q27 contains a cluster of developmental genes that operate in a concerted fashion.

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TABLE I. Two-Point Linkage Analysis of TAS to Xq25-27 Markers

	Recombination fraction									
	0.00	0.01	0.05	0.10	0.20	0.30	0.40	θ max	Z max	References#
DXS1047	$-\infty$	5.33	5.54	5.21	4.14	2.79	1.32	0.04	5.57	Gyapay et al. [1994]
HPRT	$-\infty$	5.22	5.48	5.21	4.26	3.03	1.58	0.04	5.50	Hearne and Todd [1991]
DXS994	$-\infty$	4.82	5.11	4.87	4.00	2.85	1.50	0.04	5.12	Weissenbach et al. [1992]
DXS1192	$-\infty$	4.11	4.41	4.20	3.38	2.30	1.10	0.04	4.42	Gyapay et al. [1994]
DXS102	$-\infty$	4.81	5.09	4.83	3.92	2.73	1.36	0.04	5.10	Gedeon et al. [1992]
F9	$-\infty$	3.38	3.79	3.69	3.11	2.27	1.23	0.06	3.79	Graham et al. [1991][a]
DXS1232	5.49	5.41	5.10	4.66	3.72	2.64	1.41	0.00	5.49	Gyapay et al. [1994]
DXS984	6.36	6.25	5.83	5.27	4.06	2.71	1.27	0.00	6.36	Weissenbach et al. [1992]
DXS1205	$-\infty$	3.75	4.06	3.85	3.10	2.20	1.19	0.04	4.06	Gyapay et al. [1994]
DXS1227	$-\infty$	4.57	4.84	4.58	3.66	2.45	1.04	0.04	4.86	Gyapay et al. [1994]

[a] Taq I polymorphism.

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